Therapy response was not altered by HLA-Cw6 status in psoriasis patients treated with secukinumab: a retrospective case series

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Abstract: Physicians can treat psoriasis patients with several effective treatments, however the response is individual and even the most effective therapies do sometimes not lead to a success of treatment. Currently, possible genetic markers that can predict individual therapy response are investigated. Up to now 45 genes have been identified to be associated with psoriasis [1].

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Therapy response was not altered by HLA-Cw6 status in psoriasis patients treated with secukinumab: a retrospective case series.

Running head: HLA-Cw6 status in psoriasis patients under Secukinumab

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To the Editor

Physicians can treat psoriasis patients with several effective treatments, however the response is individual and even the most effective therapies do sometimes not lead to a success of treatment. Currently, possible genetic markers that can predict individual therapy response are investigated.

Up to now 45 genes have been identified to be associated with psoriasis [1]. Of all genes, HLA-C*06, or also known as HLA-Cw6 or PSORS1 displays the strongest association [2]. This allotype is not only a risk factor for psoriasis, but has also been found of use in predicting therapy responses. Previous studies had shown a higher response rate of HLA-Cw6+ patients for TNF-alpha [3], methotrexate [4] and especially ustekinumab [5-7]. Li et al. analysed 523 patients [5]. HLA-Cw6+ patients tended to have a higher response rate to ustekinumab. This difference was however only modest and potentially of limited clinical utility. Most clinical centers including tertiary referral centers do not tend to accumulate hundreds of moderate-to-severe psoriasis patients treated with a single drug. Therefore, it is of interest to investigate whether the screening of HLA-Cw6 is of clinical utility in a day-to-day clinic. If so, we hypothesized, prescreening could possibly enhance patient care and aid clinical treatment decisions.

The patients presented to our clinic between 1 January 2010 and 31 March 2017 were included after signing an informed consent. We retrospectively collected HLA-genotyping data from patients. Genomic DNA was isolated from ethylenediamine tetraacetic acid

(EDTA) tubes with venous blood. The samples were genotyped using a primer-specific polymerase chain reaction (Olerup HLA-C*06-SSP® product number 101.614-12u, Vienna, Austria).

Secukinumab was administered in the standard doses and treatment responses were measured at 3 months by PASI.

18 patients (7 women, 11 men) were included in this retrospective study. On average, the patients were 46.4 ± 9.5 (21-61) years old and the PASI at baseline was 8.2 points. 10 patients were positive for the HLA-Cw6 allele, 8 were negative.

The majority of patients in both groups reached PASI 50 (Table 1), but not PASI 75 or PASI 90. The average PASI improvement was 74.2% (Cw6+) vs. 62.4% (Cw6-), showing no significant difference (p= 0.397) between these two groups (Figure 1).

On average, our patients had a lower PASI baseline than in comparable studies. In randomized, clinical trials patients tend to have a higher PASI since patients need to be treatment naïve or have not performed treatment for a certain amount of time. Our real life data includes patients that had previously been treated - even with other biologics - explaining this lower baseline PASI.

Even though we did not find significant differences in our small cohort, a larger trial might indeed show a statistical difference. Using the published data for predicting success of ustekinumab at 16 weeks with HLA-Cw6 [5], a power analysis ($\alpha = 0.05$, power= 90%) shows that overall 216 patients would be needed to confirm such a difference. As most centers treat their patients with a variety of anti-psoriasis drugs, the average amount of patients under secukinumab per clinic will be usually way below this number. In addition, other than for purposes of treatment response prediction, routine HLA-Cw6 testing might not be justified from a health economy perspective. We believe that for a tertiary hospital with less than 20 patients treated with secukinumab, this statistical difference is not actionable and of relevance to patients. Therefore, even though larger studies could in the future demonstrate a statistical tendency for differential treatment responses for secukinumab in certain HLA allotypes, HLA-Cw6 testing might not be warranted at this time.

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Tables and Figure legends

Table 1.

Patients' characteristiscs, PASI at baseline and treatment response.

Figure 1.

Treatment response after 12 weeks.

Table 1.

Patients' characteristiscs, PASI at baseline and treatment response.

	all	Cw6+	Cw6-
Patients (n)	18	10	8
Age	46.4 ± 9.5 (21-61)	46 ± 6.67 (21-61)	47 ± 12.86 (33-53)
Sex			
Male	12	7	5
Female	8	3	5
PASI at baseline	8.2 ± 6.3 (0-26.7)	8.65 ± 4.9 (0-17.8)	7.73 ± 8.4 (0-26.7)
PASI ≤5	5	2	3
PASI 5-10	7	3	4
PASI ≥ 10	6	5	1
Treatment response			
PASI 50	11	6 (10)	5 (8)
PASI 75	10	5 (10)	5 (8)
PASI 90	5	3 (10)	2 (8)
Average PASI improvement	64.96 ± 36.83	74.2% ± 36.1	62.4% ± 39.8